RENOGRAFIN-60 - diatrizoate meglumine and diatrizoate sodium injection, solution
Bracco Diagnostics Inc.

NOT FOR INTRATHECAL USE

DESCRIPTION

Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) is a radiopaque contrast agent supplied as a sterile, aqueous solution. Each mL provides 520 mg diatrizoate meglumine and 80 mg diatrizoate sodium; at manufacture, 3.2 mg sodium citrate and 0.4 mg edetate disodium are added per mL. The pH has been adjusted between 6.0 and 7.7 with sodium hydroxide and diatrizoic acid. *Each mL of solution also contains approximately 3.76 mg (0.16 mEq) sodium* and 292.5 mg organically bound iodine. At the time of manufacture, the air in the container is replaced by nitrogen.

CLINICAL PHARMACOLOGY

Following intravascular injection, Renografin-60 is rapidly transported through the bloodstream to the kidneys and is excreted unchanged in the urine by glomerular filtration. When urinary tract obstruction is severe enough to block glomerular filtration, the agent appears to be excreted by the tubular epithelium.

Certain applications of the contrast agent make use of the natural physiologic mechanism of excretion. Thus, the intravenous injection of the agent permits visualization of the kidneys and urinary passages.

Renal accumulation is sufficiently rapid that the period of maximal opacification of the renal passages may begin as early as five minutes after injection. In infants and small children excretion takes place somewhat more promptly than in adults, so that maximal opacification occurs more rapidly and is less sustained. The normal kidney eliminates the contrast medium almost immediately.

In nephropathic conditions, particularly when excretory capacity has been altered, the rate of excretion varies unpredictably, and opacification may be delayed for 30 minutes or more after injection; with severe impairment opacification may not occur. Generally, however, the medium is concentrated in sufficient amounts and promptly enough to permit a thorough evaluation of the anatomy and physiology of the urinary tract. After intramuscular injection, the contrast agent is promptly absorbed and normally reaches the renal passages within 20 to 60 minutes.

Intravascular injection of diatrizoate also opacifies those vessels in the path of flow of the medium, permitting visualization until the circulating blood dilutes the concentration of the medium. Thus selective angiography may be performed following injection directly into veins or arteries such as the carotid, the vertebral, or the vessels of the extremities.

Under certain circumstances, specific parts of the body which do not concentrate the contrast agent physiologically may be visualized by injecting the agent directly into the region to be studied. The biliary tract is one organ system which may be visualized in this manner. In operative cholangiography, injection of the radiopaque medium into the cystic duct or choledochal lumen, at laparotomy, opacifies the intra- and extra-hepatic biliary ductal system, revealing the nature and location of obstructions such as stones or strictures. Injection of the medium through an in-place T-tube, immediately after exploration of the common duct, permits the visualization of retained stones. A repetition of “T-tube cholangiography,” performed as part of the postoperative follow-up, insures the patency of the ductal system before removal of the T-tube. The biliary ductal system may also be opacified by the percutaneous transhepatic route. In relatively long-standing biliary obstruction, the biliary ducts are usually enlarged sufficiently to be located promptly by percutaneous transhepatic probing, permitting injection of the contrast agent directly into the biliary ductal system.

If the contrast agent is injected directly into the splenic pulp, significant opacification of the splenic and portal veins is obtained. Because of gravity, the dependent portions of the portal system are better opacified than the superior portions. The agent is carried from the portal vein into the hepatic veins, and a diffuse opacification of the liver results. In patients with portal hypertension, collateral pathways caused by the change in portal blood flow may be visualized and esophageal varices are often delineated. The procedure may reveal the site of portal obstruction.

Injection of Renografin-60 directly into a joint space provides visual information about joint derangements.

A small amount of the radiopaque agent injected into a normal cervical or lumbar disk will, under optimal conditions, concentrate within the nucleus pulposus. In the presence of disk pathology the injected agent may reveal significant bulging or disruption of the annulus beyond its normal confines and may identify disk degeneration, retropulsion, or rupture.

Computed Tomography

Renografin-60 enhances computed tomographic brain scanning through augmentation of radiographic efficiency. The degree of enhancement of visualization of tissue density is directly related to the iodine content in an administered dose; peak iodine blood levels occur immediately following rapid injection of the dose. These levels fall rapidly within five to ten minutes.This can be accounted for by the dilution in the vascular and extracellular fluid compartments which causes an initial sharp fall in plasma concentration. Equilibration with the extracellular compartments is reached in about ten minutes; thereafter, the fall becomes exponential. Maximum contrast enhancement frequently occurs after peak blood iodine levels are reached. The delay in maximum contrast enhancement can range from five to forty minutes, depending on the peak iodine levels achieved and the cell type of the lesion. This lag suggests that radiographic contrast enhancement is at least in part dependent on the accumulation of iodine within the lesion and outside the blood pool, although the mechanism by which this occurs is not clear. The radiographic enhancement of

nontumoral lesions, such as arteriovenous malformations and aneurysms is probably dependent on the iodine content of the circulating blood pool.
In brain scanning, Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) does not accumulate in normal brain tissue due to the presence of the "blood-brain" barrier. The increase in X-ray absorption in normal brain is due to the presence of contrast agent within the blood pool. A break in the blood-brain barrier such as occurs in malignant tumors of the brain allows the accumulation of the contrast medium within the interstitial tumor tissue. Adjacent normal brain tissue does not contain the contrast medium.
In nonneural tissues (during computed tomography of the body), diatrizoate diffuses rapidly from the vascular into the extravascular space. Increase in X-ray absorption is related to blood flow, concentration of the contrast medium, and extraction of the contrast medium by interstitial tumor tissue since no barrier exists. Contrast enhancement is thus due to the relative differences in extravascular diffusion between normal and abnormal tissue, quite different from that in the brain.
The pharmacokinetics of diatrizoate in both normal and abnormal tissue have been shown to be variable. Contrast enhancement appears to be greatest soon after administration of the contrast medium, and following intra-arterial rather than intravenous administration. Thus, greatest enhancement can be detected by a series of consecutive two- to three-second scans performed just after injection (within 30 to 90 seconds), i.e., dynamic computed tomographic scanning.

INDICATIONS
Renografin-60 is indicated in excretion urography (by direct I.V. or drip infusion); cerebral angiography; peripheral arteriography; venography; operative, T-tube, or percutaneous transhepatic cholangiography; splenoportography; arthrography; and discography.

Computed Tomography
Renografin-60 is also indicated for radiographic contrast enhancement in computed tomography (CT) of the brain and body. Contrast enhancement may be advantageous in delineating or ruling out disease in suspicious areas which may otherwise not have been satisfactorily visualized.

Brain Tumors
Renografin-60 may be useful to demonstrate the presence and extent of certain malignancies such as: gliomas including malignant gliomas, glioblastomas, astrocytomas, oligodendrogliomas and gangliomas; ependymomas; medulloblastomas; meningiomas; neuromas; pinealomas; pituitary adenomas; craniopharyngiomas; germinomas; and metastatic lesions.

The usefulness of contrast enhancement for the investigation of the retrobulbar space and in cases of low grade or infiltrative glioma has not been demonstrated. In cases where lesions have calcified, there is less likelihood of enhancement. Following therapy, tumors may show decreased or no enhancement.

Non-Neoplastic Conditions of The Brain
The use of Renografin-60 may be beneficial in the enhancement of images of lesions not due to neoplasms. Cerebral infarctions of recent onset may be better visualized with the contrast enhancement, while some infarctions are obscured if a contrast medium is used. The use of Renografin-60 improved the contrast enhancement in approximately 60 percent of cerebral infarctions studied from one week to four weeks from the onset of symptoms.

Sites of active infection also will produce contrast enhancement following contrast medium administration.

Arteriovenous malformations and aneurysms will show contrast enhancement. In the case of these vascular lesions, the enhancement is probably dependent on the iodine content of the circulating blood pool.

Hematomas and intraparenchymal bleeders seldom demonstrate any contrast enhancement. However, in cases of intraparenchymal clot, for which there is no obvious clinical explanation, contrast medium administration may be helpful in ruling out the possibility of associated arteriovenous malformation.

The opacification of the inferior vermis following contrast medium administration has resulted in false-positive diagnoses in a number of normal studies.

Body Scanning
Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) maybe used for enhancement of computed tomographic scans performed for detection and evaluation of lesions in the liver, pancreas, kidneys, aorta, mediastinum, abdominal cavity, pelvis and retroperitoneal space.

Enhancement of computed tomography with Renografin-60 may be of benefit in establishing diagnoses of certain lesions in these sites with greater assurance than is possible with CT alone, and in supplying additional features of the lesions (e.g., hepatic abscess delineation prior to percutaneous drainage). In other cases, the contrast agent may allow visualization of lesions not seen with CT alone (e.g., tumor extension), or may help to define suspicious lesions seen with unenhanced CT (e.g., pancreatic cyst).

Contrast enhancement appears to be greatest within 60-90 seconds after bolus administration of the contrast agent. Therefore, utilization of a continuous scanning technique ("dynamic CT scanning") may improve enhancement and diagnostic assessment of tumor and other lesions such as an abscess, occasionally revealing unsuspected or more extensive disease. For example, a cyst may be distinguished from a vascularized solid lesion when precontrast and enhanced scans are compared; the non-perfused mass shows unchanged X-ray absorption (CT number). A vascularized lesion is characterized by an increase in CT number in the few minutes after a bolus of intravascular contrast agent; it may be malignant, benign or normal tissue, but would probably not be a cyst, hematoma, or other nonvascular lesion.

Because unenhanced scanning may provide adequate diagnostic information in the individual patient, the decision to employ contrast enhancement, which may be associated with risk and increased radiation exposure, should be based upon a careful evaluation of clinical, other radiological, and unenhanced CT findings.

CONTRAINDICATIONS

Renografin-60 is contraindicated for use in intrathecal procedures. This preparation is contraindicated in patients with a hypersensitivity to salts of diatrizoic acid.

Urography is contraindicated in patients with anuria.

Specific contraindications to **percutaneous transhepatic cholangiography** include a prothrombin time below 50 percent and evidence of coagulation defects.

Splenoportography should not be performed on any patient for whom splenectomy is contraindicated, since complications of the procedure at times make splenectomy necessary. Other contraindications include prothrombin time below 50 percent, significant thrombocytopenia or coagulation defect, and any condition which may increase the possibility of rupture of the spleen.

Arthrography should not be performed if infection is present in or near the joint.

Discography should not be performed in patients with an infection or open injury near the region to be examined.

WARNINGS

Severe Adverse Events — Inadvertent Intrathecal Administration

Serious adverse reactions have been reported due to the inadvertent intrathecal administration of iodinated contrast media that are not indicated for intrathecal use. These serious adverse reactions include: death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema. Special attention must be given to insure that this drug product is not inadvertently administered intrathecally.

The possibility exists for inadvertent administration into the intrathecal space during epidural administrations. Therefore, epidural administration procedures, such as pain management catheter placement, should not be performed with use of this product.

General

Ionic iodinated contrast media inhibit blood coagulation, *in vitro*, more than nonionic contrast media. Nonetheless, it is prudent to avoid prolonged contact of blood with syringes containing ionic contrast media.

Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both ionic and nonionic contrast media. Therefore, meticulous intravascular administration technique is necessary, particularly during angiographic procedures, to minimize thromboembolic events. Numerous factors, including length of procedure, catheter and syringe material, underlying disease state, and concomitant medications may contribute to the development of thromboembolic events. For these reasons, meticulous angiographic techniques are recommended including close attention to guidewire and catheter manipulation, use of manifold systems and/or three way stopcocks, frequent catheter flushing with heparinized saline solutions, and minimizing the length of the procedure. The use of plastic syringes in place of glass syringes has been reported to decrease but not eliminate the likelihood of *in vitro* clotting.

A definite risk exists in the use of intravascular contrast agents in patients who are known to have multiple myeloma. In such instances there has been anuria resulting in progressive uremia, renal failure, and eventually death. Although neither the contrast agent nor dehydration has separately proved to be the cause of anuria in myeloma, it has been speculated that the combination of both may be the causative factor. The risk in myelomatous patients is not a contraindication to the procedures; however, partial dehydration in the preparation of these patients for the examination is not recommended since this may predispose to the precipitation of myeloma protein in the renal tubules. No form of therapy, including dialysis, has been successful in reversing this effect. Myeloma, which occurs most commonly in persons over age 40, should be considered before intravascular administration of a contrast agent.

Administration of radiopaque materials to patients known or suspected to have pheochromocytoma should be performed with extreme caution. If, in the opinion of the physician, the possible benefits of such procedures outweigh the considered risks, the procedures may be performed; however, the amount of radiopaque medium injected should be kept to an absolute minimum. The blood pressure should be assessed throughout the procedure and measures for treatment of a hypertensive crisis should be available.

Contrast media have been shown to promote the phenomenon of sickling in individuals who are homozygous for sickle cell disease when the material is injected intravenously or intra-arterially.

Since iodine-containing contrast agents may alter the results of thyroid function tests, such tests, if indicated, should be performed prior to the administration of this preparation.
A history of sensitivity to iodine *per se* or to other contrast agents is not an absolute contraindication to the use of diatrizoate but calls for extreme caution in administration.
Avoid accidental introduction of this preparation into the subarachnoid space since even small amounts may produce convulsions and possible fatal reactions. In patients with subarachnoid hemorrhage, a rare association between contrast administration and clinical deterioration, including convulsions and death, has been reported; therefore, administration of intravascular iodinated ionic contrast media in these patients should be undertaken with caution.
Cerebral angiography should be undertaken with special caution in extreme age, poor clinical condition, advanced arteriosclerosis, severe arterial hypertension, cardiac decompensation, recent cerebral embolism, or thrombosis.
Urography should be performed with extreme caution in patients with severe concomitant hepatic and renal disease.

PRECAUTIONS
Diagnostic procedures which involve the use of radiopaque diagnostic contrast agents should be carried out under the direction of personnel with the prerequisite training and with a thorough knowledge of the particular procedure to be performed. Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reactions to the contrast agent itself. After parenteral administration of a radiopaque agent, competent personnel and emergency facilities should be available for at least 30 to 60 minutes since severe delayed reactions have occured (see **ADVERSE REACTIONS**).
Severe, life-threatening reactions suggest hypersensitivity to the radiopaque agent, which has prompted the use of several pretesting methods, none of which can be relied upon to predict severe reactions. Many authorities question the value of any pretest. A history of bronchial asthma or allergy, a family history of allergy, or a previous reaction to a contrast agent warrant special attention. Such a history, by suggesting histamine sensitivity and a consequent proneness to reactions, may be more accurate than pretesting in predicting the likelihood of a reaction, although not necessarily the severity or type of reaction in the individual case.
The sensitivity test most often performed is the slow injection of 0.5 to 1.0 mL of the radiopaque medium, administered intravenously, prior to injection of the full diagnostic dose. It should be noted that the absence of a reaction to the test dose does not preclude the possibility of a reaction to the full diagnostic dose. If the test dose causes an untoward response of any kind, the necessity for continuing with the examination should be carefully reevaluated and, if it is deemed essential, the examination should be conducted with all possible caution. In rare instances, reactions to the test dose itself may be extremely severe; therefore, close observation of the patient, and facilities for emergency treatment, appear indicated.
Renal toxicity has been reported in a few patients with liver dysfunction who were given oral cholecystographic agents followed by urographic agents. Administration of Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) should therefore be postponed in any patient with a known or suspected hepatic or biliary disorder who has recently taken a cholecystographic contrast agent.
Caution should be exercised with the use of radiopaque media in severely debilitated patients and in those with marked hypertension.
The possibility of thrombosis should be borne in mind when percutaneous techniques are employed.
Consideration must be given to the functional ability of the kidneys before injecting this preparation.
Contrast agents may interfere with some chemical determinations made on urine specimens therefore, urine should be collected before administration of the contrast medium or two or more days afterwards.
The following precautions pertain to specific procedures:
Peripheral arteriography: Hypotension or moderate decreases in blood pressure seem to occur frequently with intra-arterial (brachial) injections; therefore, the blood pressure should be monitored during the immediate ten minutes after injection; this blood pressure change is transient and usually requires no treatment.
Excretion urography: Adequate visualization may be difficult or impossible to attain in uremic patients or others with severely impaired renal function (see **CONTRAINDICATIONS**). The increased osmotic load associated with drip infusion pyelography should be considered in patients with congestive heart failure. The diuretic effect of the drip infusion pyelography procedure may hinder assessment of residual urine in the bladder. The recommended rate of infusion should not be exceeded.
Acute renal failure has been reported in diabetic patients with diabetic nephropathy and susceptible nondiabetic patients (often elderly with preexisting renal disease) following excretion urography, Therefore, careful consideration should be given before performing this procedure in these patients.
Operative and T-tube cholangiography: Injection should be made slowly to prevent extravasation of the medium into the peritoneal cavity, and to minimize reflux flow into the pancreatic duct which may result in pancreatic irritation.
Percutaneous transhepatic cholangiography: To reduce the possibility of bile leakage and consequent peritonitis, as much of the contrast agent as possible should be aspirated on completion of successful films. All patients should be carefully and constantly monitored for 24 hours after the procedure for signs of internal hemorrhage or bile leakage; if these complications are recognized immediately, remedial measures can be instituted promptly with minimal increase in morbidity. Percutaneous transhepatic cholangiography is not without risk and should therefore be reserved for special circumstances when ordinary studies of the biliary system have failed to provide the requisite information in jaundiced patients who are not good candidates for surgery. The procedure should only be attempted when competent surgical intervention can be promptly obtained if needed.

Splenoportography: It is best to avoid manipulations which would prolong the time the needle is in the spleen, since they may contribute to subcapsular extravasation of the contrast agent, and also to postpuncture bleeding. Following splenoportography, the patient should lie on his left side for several hours and should be closely observed for 24 hours for signs of internal bleeding, which is the most common complication of the procedure. Fatal hemorrhage has occurred on rare occasion, but leakage of up to 300 mL of blood from the spleen is apparently not uncommon. Blood transfusions may be required, and rarely splenectomy.
Discography: To minimize the possibility of introducing infection, discography should be postponed in any patient with an infection or open injury near the region to be examined, including upper respiratory infections in the case of cervical discography. All possible care should be taken to preclude contamination and resultant infection of the disk, which has been reported after discography. In cervical discography, particular care is needed to avoid puncturing the esophagus and thereby introducing contamination into the disk. Rupture of the disk is highly unlikely if care in performance is observed, but may occur if the point of the needle has been barbed by contact with bone; use of the two-needle technique should help reduce this hazard.

USAGE IN PREGNANCY
Safety for use during pregnancy has not been established; therefore, this preparation should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

ADVERSE REACTIONS
Mild, moderate, and sometimes severe adverse reactions may occur associated with the procedure and/or the contrast media. Reactions known to occur with parenteral administration of iodinated ionic contrast media (see the listing below) are possible with a nonionic agent. Approximately 95 percent of adverse reactions accompanying the use of other water-soluble intravascularly administered contrast agents are mild to moderate in degree. However, severe and life-threatening reactions and fatalities, mostly of cardiovascular origin, have occurred.
Reported incidences of death from the administration of other iodinated contrast media range from 6.6 per 1 million (0.00066 percent) to 1 in 10,000 patients (0.01 percent). Most deaths occur during injection or 5 to 10 minutes later, the main feature being cardiac arrest with cardiovascular disease as the main aggravating factor. Isolated reports of hypotensive collapse and shock are found in the literature. The incidence of shock is estimated to be 1 out of 20,000 (0.005 percent) patients.
Nausea, vomiting, flushing, or a generalized feeling of warmth are the reactions seen most frequently with intravascular injection. Symptoms which may occur are chills, fever, sweating, headache, dizziness, pallor, weakness, severe retching and choking, wheezing, a rise or fall in blood pressure, facial or conjunctival petechiae, urticaria, pruritus, rash, and other eruptions, edema, cramps, tremors, itching, sneezing, lacrimation, etc. Antihistaminic agents may be of benefit; rarely such reactions may be severe enough to require discontinuation of dosage.
Severe reactions which may require emergency measures may take the form of a cardiovascular reaction characterized by peripheral vasodilatation with resultant hypotension and reflex tachycardia, dyspnea, agitation, confusion and cyanosis progressing to unconsciousness. Or, the histamine-liberating effect of these compounds may induce an allergic-like reaction which may range in severity from rhinitis or angioneurotic edema to laryngeal or bronchial spasm or anaphylactoid shock.
Temporary renal shutdown or other nephropathy may occur. Temporary neurologic effects of varying severity have occurred in a few instances, particularly when the medium was used for angiography in the diagnosis of cerebral pathology. Although local tissue tolerance is usually good, there have been a few reports of a burning or stinging sensation or numbness and of venospasm or venous pain, and partial collapse of the injected vein. Neutropenia or thrombophlebitis may occur.
Adverse effects may sometimes occur as a consequence of the procedure for which the contrast agent is used. Adverse reactions in**excretion urography** have included cardiac arrest, ventricular fibrillation, anaphylaxis with severe asthmatic reaction, and flushing due to generalized vasodilation. **Cerebral angiography** has been known to cause temporary neurologic complications such as induction of seizures, particularly in patients with convulsive disorders; confusional states or drowsiness; transient paresis; coma; temporary disturbances in vision; or seventh nerve weakness. During **peripheral arteriography**, complications have occurred including hemorrhage from the puncture site, thrombosis of the vessel, and brachial plexus palsy following axillary artery injections. Complications of **percutaneous transhepatic cholangiography** have been estimated to occur in four to six percent of cases and have included bile leakage and biliary peritonitis, gall-bladder perforation, internal bleeding, septicemia involving gram-negative organisms, and tension pneumothorax from inadvertent puncture of the diaphragm and lung. Bile leakage may be more likely in patients with complete obstruction due to carcinoma.
During **splenoportography,** intraperitoneal extravasation of the contrast medium may cause transient diaphragmatic irritation or mild to moderate transient pain which may sometimes be referred to the shoulder, the periumbilical region, or other areas. Because of the proximity of the pleural cavity, accidental pneumothorax has been known to occur. Inadvertent injection of the medium into other nearby structures is not likely to cause untoward consequences.
Arthrography may induce joint pain or increase existing pain, particularly if a large dose is used and the medium extravasates into surrounding soft tissue. Pain or discomfort is usually immediate and transient but may be delayed or of extended duration (up to 24 hours). Lipid-filled histiocytes have been found in tissue removed following arthrography. The technique of **discography** may be painful, particularly when disk pathology exists. Pain on injection may also be related to the volume of the dose. The nature of the disk pathology or extravasation of contrast agent may cause referred pain.
When any percutaneous technique is employed the possibility of thrombosis or of other complications due to the mechanical trauma of the procedure should be borne in mind.

DOSAGE AND ADMINISTRATION
Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) should be at body temperature when injected, and may need to be warmed before use. If kept in a syringe for prolonged periods before injection, it should be protected from exposure to strong light.
Dilution and withdrawal of the contrast agent should be accomplished under aseptic conditions with sterile needle and syringe.

Excretion Urography
Appropriate preparation of the patient is desirable for optimal results. In adults and older children, a laxative the night before the examination, a low residue diet the day before, and low liquid intake for 12 hours prior to the procedure may be used to clear the gastrointestinal tract and to induce a partial dehydration which is believed to increase the urinary concentration of the contrast medium. Preparatory partial dehydration is not recommended in infants, young children, the elderly, or azotemic patients (especially those with polyuria, oliguria, diabetes, advanced vascular disease, or preexisting dehydration). The undesirable dehydration in these patients may be accentuated by the osmotic diuretic action of the medium.
In uremic patients partial dehydration is not necessary and maintenance of adequate fluid intake is particularly desirable.

Direct I.V. Injection: The dose range for adults is 25 to 50 mL; the usual dose is 25 mL; children require proportionately less. Suggested dosages are as follows: Under 6 months-5 mL; 6 to 12 months-8 mL; 1 to 2 years-10 mL; 2 to 5 years-12 mL; 5 to 7 years-15 mL; 8 to 10 years-18 mL; 11 to 15 years-20 mL; adults (16 years and older)-25 to 50 mL. In adults, when the smaller dose has provided inadequate visualization, or when poor visualization is anticipated, the 50 mL dose may be given. Drip infusion may be used when direct I.V. pyelography is not expected to be or has not been satisfactory (see below).

The preparation is given by intravenous injection. If flushing or nausea occurs during administration, injection should be slowed or briefly interrupted until the side effects have disappeared.

A scout film should be made before the contrast medium is administered. To allow for individual variation, several films should be exposed beginning approximately five minutes after injection. In patients with renal dysfunction optimal visualization may be delayed until 30 minutes or more after injection.

NOTE: In infants and children and in certain adults the medium may be injected intramuscularly. The suggested dose is 25 mL for adults and proportionately less for children, divided and given bilaterally in the gluteal muscles. Radiographs should be taken at 20, 40, and 60 minutes after the medium is injected.

Drip Infusion Pyelography: In drip infusion pyelography, the recommended dose of Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) is calculated on the basis of 1 mL of Renografin-60 per pound of body weight diluted with an equal volume of Sterile Water for Injection USP. The diluted preparation (30%) is given by I.V. infusion through a large bore (17- to 18-gauge) needle at a rate of 40 mL per minute. The recommended rate of infusion should not be exceeded and the total volume administered should generally not exceed 300 mL. In older patients and in patients with known or suspected cardiac decompensation, a slower rate of infusion is probably wise.

If nausea or flushing occurs during administration, the infusion should be slowed or briefly interrupted.

Films are taken before the onset of the infusion and at the desired intervals following its completion. When renal function is normal, a nephrogram may be taken as soon as the infusion is completed, and films of the collecting system at 10 and 20 minutes thereafter. Voiding cystourethrograms are usually optimal at 20 minutes after the infusion is completed. In hypertensive patients, early minute sequence films may be taken during the course of infusion, in addition to subsequent pyelograms. In patients with renal dysfunction, optimal visualization is usually delayed, and late films are taken as indicated.

The nephrogram obtained by the drip infusion procedure may be dense enough to obscure the pelvocalyceal system in some cases. The presence of gas in the bowel may hamper early visualization of the renal collecting system. Tomographic “cuts” may help to overcome such difficulties.

Nephrotomography may begin when the infusion is completed. The sustained contrast achieved by the drip infusion technique eliminates the need for precise timing and teamwork that is necessary with ordinary nephrotomography. Thus, if nephrograms taken after infusion of the medium suggest the need for sectional films, or if preselected tomographic “cuts” are not sufficient, additional tomograms may be obtained at once, and without repetition of dosage.

Cerebral Angiography
Appropriate preparation of the patient is indicated, including suitable premedication. The average single dose for adults is 10 mL, repeated as indicated. Children require less in proportion to weight.
Either the percutaneous or operative method of administration may be used. For visualization of the cerebral vessels, the contrast medium is injected into the common carotid artery; for angiography of the vessels in the posterior fossa or the occipital lobes, the

medium is injected into the vertebral artery. Since the medium is given by rapid injection, the patient should be watched for untoward reactions. Unless general anesthesia is used, patients should be warned that the medium may provoke movement and that they may feel transient pain, flushing, or burning during the injection.
A scout film should be made routinely before the contrast medium is injected. Serial films begun while the last few mL are being injected should permit visualization of the arterial, intermediate, and venous phases.

Peripheral Arteriography
Appropriate preparation of the patient is indicated, including suitable premedication. For visualization of an entire extremity, a single dose of 20 to 40 mL is suggested; for the upper or lower half of the extremity only, 10 to 20 mL is usually sufficient.
Injection is made into the femoral or subclavian artery by the percutaneous or operative method. Because the contrast agent is given by rapid injection, flushing of the skin may occur. Patients not under general anesthesia may experience nausea and vomiting or a transient feeling of warmth. Vascular spasm is not likely to occur.
A scout film should be made routinely before administering the contrast medium. Radiograms of the upper half of the extremity are taken while the last few mL are being injected, followed by radiograms of the lower half of the extremity a few seconds later.

Venography
For visualization of veins in the upper extremities, a single dose of 10 mL per extremity is suggested. For veins in the lower extremities, doses of 20 to 40 mL per extremity are suggested. In exceptional circumstances, larger doses may be necessary; visualization of the iliac vein, extensive varicosities or large veins may require 50 mL or more. Total doses up to 100 mL per lower extremity have been used safely.
For visualization of an upper extremity, the medium may be given by percutaneous injection into any convenient superficial vein of the forearm or hand. For the visualization of a lower extremity it should be injected into a superficial vein on the lateral side of the foot. The medium is injected rapidly; patients should be observed for untoward reactions.
Radiograms are taken when injection is completed; sufficient time should be allowed to permit diffusion of the contrast medium.

Operative and Postoperative Cholangiography
Operative cholangiography is performed as soon as the gallbladder and ducts have been exposed surgically. The usual dose is 10 mL but as much as 25 mL may be needed, depending on the caliber of the ducts. If desired, the contrast agent may be diluted 1:1 with Sodium Chloride Injection USP under strict aseptic procedures.
The contrast medium is instilled slowly through the stump of the cystic duct or directly into the choledochal lumen. Following surgical exploration of the ductal system, repeat studies may be performed before closure of the abdomen, using the same dose as before.
Postoperatively, the ductal system may be examined by injection of the contrast agent through an in-place T-tube. “T-tube cholangiography” is usually performed eight to ten days after operation; the usual dose is the same as for operative cholangiography.
For each procedure, films are taken immediately after instillation of the medium and are read immediately. Additional films are then taken if necessary.

Percutaneous Transhepatic Cholangiography
Facilities for emergency surgery should be available whenever this examination is performed. Appropriate premedication of the patient is recommended; drugs which are likely to cause spasm, such as morphine, should be avoided.
Depending on the caliber of the biliary tree, a dose of 20 to 40 mL is generally sufficient to opacify the entire ductal system. The contrast agent may be diluted 1:1 with Sodium Chloride Injection USP, if desired, under strict aseptic procedures.
Injection is made into a biliary duct by the percutaneous transhepatic method. Before the dose is administered, as much bile as possible is aspirated. The medium is then slowly injected into the duct under very slight pressure. If a duct is not located promptly, successive small doses of 1 to 2 mL are injected into the liver as the needle is gradually withdrawn, until a duct is visualized by x-ray. If no duct can be located after three or four attempts, the procedure is abandoned.
Serial films are taken rapidly during and after injection of the medium into the biliary ducts. Repositioning of the patient, if necessary, should be done with care.
In hepatocellular disease, the biliary ducts are generally not enlarged and cannot successfully be opacified by this method. Thus, in the presence of long-standing jaundice, failure to obtain a successful percutaneous transhepatic cholangiogram by a person experienced in the technique is generally considered to be strongly suggestive of nonobstructive or hepatocellular-type jaundice.

Splenoportography
Prior gastrointestinal x-ray examination should include particular attention to the lower esophageal area. A hematologic survey, including prothrombin time and platelet count, should be performed. The patient should have no food for several hours and should be mildly sedated. Splenoportography is usually performed under local anesthesia.
Approximately 20 to 25 mL of the contrast agent is usually adequate. The dose is injected rapidly, following radiologic location and percutaneous puncture of the spleen.
Preliminary films are taken to locate the spleen before the injection is begun. Rapid serial films are then started simultaneously with injection of the dose. Serial films are necessary since the entire portal system cannot be captured on a single film and also because of individual variations in portal circulation time.

Arthrography
The amount of contrast agent required is dependent on the size of the joint to be injected. For an adult, the following doses are generally suitable: knee-5 to 15 mL; shoulder or hip-5 to 10 mL; other joints-1 to 4 mL. Dosage for children should be suitably reduced.
The injection site should be prepared aseptically. Excessive synovial fluid should be aspirated to minimize pain and to reduce intra-articular dilution of the contrast agent. If indicated, the agent may be administered under local anesthesia. After injection of the medium, the joint should be manipulated gently in order to spread the medium throughout the joint space. In some instances, double contrast arthrography, injecting both air and contrast medium, has been of value.
Films are taken from several angles; stereoscopic films may be advantageous.
When the contrast agent is used to opacify a joint space, much of the agent may be aspirated at the end of the procedure.

Discography
No prior preparation of the patient is required, although administration of an analgesic or sedative 20 minutes before the procedure may be helpful. Discography is performed under local anesthesia using the usual aseptic precautions.
Dosage is generally determined by the amount of contrast agent which can easily be injected into the disk without force. A cervical disk will normally accept up to 0.5 mL and a lumbar disk 1 or 2 mL. The amount may vary, and injection should be discontinued when resistance is felt. The rate of injection may influence the amount which can be injected. To reduce the probability of extravasation and to minimize unnecessary pain, injection should be made slowly and not more than 2 mL should be injected into any one disk.
A two-needle technique may be used to administer the contrast medium, with a large-gauge needle to locate the disk and a small-gauge needle within the larger one to puncture the disk and administer the medium. The correct position of the two needles is established radiologically before the medium is injected.
Spot roentgenograms should be taken anteroposteriorly, obliquely, and laterally as soon as disks have been injected.
When the contrast agent is used for discography, it need not be aspirated at the end of the procedure.

Computed Tomography

Brain Scanning
The suggested dose range is 50 to 150 mL by intravenous administration; scanning may be performed immediately after completion of administration. Doses for children should be proportionately less, depending on age and weight.

Body Scanning
The usual adult dose is 100 mL administered by rapid intravenous (within approximately 1 minute) bolus injection. Scanning is performed immediately after injection.

Gastrografin® (Diatrizoate Meglumine and Diatrizoate Sodium Solution USP), an oral radiopaque contrast agent, may be useful as an adjunct to the procedure.

Patient Preparation
No special patient preparation is required for contrast enhancement of CT brain scanning or body scanning. However, it is advisable to insure that patients are well hydrated prior to examination.

HOW SUPPLIED
Renografin-60 (Diatrizoate Meglumine and Diatrizoate Sodium Injection USP) is available in packages of:
Ten 50 mL single dose vials (NDC 0270-0707-49)
Ten 100 mL single dose bottles (NDC 0270-0707-55).

STORAGE
The preparation should be stored at 20-25°C (68-77°F) [See USP], protected from light. If precipitation or solidification has occurred due to storage in the cold, immerse the container in hot water and shake intermittently to redissolve any solids.

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